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Figure <sup>21</sup>~~3~~ is a table of 741 calcium channel antagonists according to the present invention.

### DETAILED DESCRIPTION OF THE INVENTION

Biological systems in general are controlled by molecular interactions  
5 between bioactive ligands and their receptors, in which the receptor  
"recognizes" a molecule or a portion thereof (*i.e.*, a ligand domain) to  
produce a biological effect. The voltage-gated  $\text{Ca}^{++}$  channels are considered  
to be pharmacological receptors: they possess specific binding sites for  
ligands having agonist and antagonist activities; the binding of ligands to  
10 such sites allosterically modulates  $\text{Ca}^{++}$  flux through the channel; the  
channel properties (*i.e.*, gating and ion selectivity) are regulatable; and  
various channels are known to associate with G-proteins (D. Rampe and  
D.J. Triggle, *Prog. Drug Res.* 40: 191-238 (1993). Accordingly, diseases or  
conditions that involve, or are mediated by,  $\text{Ca}^{++}$  channels can be treated  
15 with pharmacologically active ligands that interact with such channels to  
initiate, modulate or abrogate transporter activity .

The interaction of a  $\text{Ca}^{++}$  channel and a  $\text{Ca}^{++}$  channel-binding ligand  
may be described in terms of "affinity" and "specificity". The "affinity" and  
"specificity" of any given ligand- $\text{Ca}^{++}$  channel interaction is dependent upon  
20 the complementarity of molecular binding surfaces and the energetic costs  
of complexation (*i.e.*, the net difference in free energy  $\Delta G$  between bound  
and free states). Affinity may be quantified by the equilibrium constant of  
complex formation, the ratio of on/off rate constants, and/or by the free  
energy of complex formation. Specificity relates to the difference in binding  
25 affinity of a ligand for different receptors.

The net free energy of interaction of such ligands with a  $\text{Ca}^{++}$  channel  
is the difference between energetic gains (enthalpy gained through  
molecular complementarity and entropy gained through the hydrophobic